EXHIBIT J

Original Investigation

Removal or Revision of Vaginal Mesh Used for the Treatment of Stress Urinary Incontinence

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IMPORTANCE Synthetic mesh slings are the most common surgical treatment for female stress urinary incontinence (SUI). However, the US Food and Drug Administration has released warnings that question the safety of vaginal mesh.

OBJECTIVES To measure the incidence of mesh removal or revision after SUI procedures and to determine whether significant surgeon and patient risk factors exist.

DESIGN, SETTING, AND PARTICIPANTS Population-based retrospective cohort study that included all adult women undergoing an incident procedure for SUI with synthetic mesh in Ontario, Canada, from April 1, 2002, through December 31, 2012 (N = 59 887). The end of potential follow-up was March 31, 2013. Data were analyzed from November 1, 2014, through February 28, 2015.

EXPOSURES Yearly volume of mesh-based procedures for SUI performed by the treating surgeons and their surgical specialty.

MAIN OUTCOMES AND MEASURES The primary outcome was a composite of surgical procedures related to removal or revision of mesh slings (owing to erosion, fistula, pain, or retention). We hypothesized a priori that surgeon volume would be inversely correlated with complications.

RESULTS Among the identified 59 887 women who underwent a mesh-based procedure for SUI, the median age was 52 (interquartile range [IQR], 45-63) years. High-volume surgeons (≥75th percentile of yearly mesh-based procedures) were less likely to perform a simultaneous hysterectomy (performed in 11.5% vs 16.5% of patients; standardized difference, 0.14), were more likely to work in an academic center (28.9% vs 16.3% of patients; standardized difference, 0.30), and saw the patient less frequently in the year before the procedure (median, 2 [IQR, 1-3] vs 3 [IQR, 2-4] visits; standardized difference, 0.26). Complications were treated in 1307 women (2.2%), and the 10-year cumulative incidence rate was 3.29 (95% CI, 3.05-3.53). In our multivariable survival model, patients of high-volume surgeons had a significantly lower risk (95% CI) for experiencing our composite outcome (hazard ratio [HR], 0.73 [0.65-0.83]; absolute risk reduction, 0.63% [0.36%-0.92%]; $P < .01$). Gynecologists were not significantly associated with more complications compared with urologists (HR, 0.94 [95% CI, 0.83-1.08]; $P = .38$). Among our secondary exposures of interest, multiple mesh-based SUI procedures increased the risk for complications (HR, 4.73 [95% CI, 3.62-6.17]; $P < .01$). However, traditional high-risk patient features did not increase the risk (HR, 0.58 [95% CI, 0.08-4.13]; $P = .59$).

CONCLUSIONS AND RELEVANCE Ten years after SUI mesh surgery, 1 of every 30 women may require a second procedure for mesh removal or revision. Patients of lower-volume surgeons have a 37% increased likelihood of having a complication. These findings support the recommendations of the US Food and Drug Administration related to the use of vaginal mesh for treatment of SUI.

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Invited Commentary

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Female stress urinary incontinence (SUI) is a common condition[1] that is often treated with surgery when conservative management options are unsuccessful. An estimated 1 in 7 women will undergo surgery for SUI during their lifetime.[2]

Synthetic mesh has been used since the 1960s for the treatment of SUI. However, the introduction of commercial midurethral sling kits in the mid-1990s led to the rapid adoption of this procedure and an overall increase of use in procedures to treat SUI.[3] Midurethral sling implants constitute the most prevalent surgical treatment for SUI, and they have supplanted previously common operations, such as retropubic suspensions and bladder-neck sling implants.[3,4] Although the efficacy is similar among all of these procedures,[5] the midurethral sling is preferable owing to a significantly shorter operative time and hospital stay and a quicker patient recovery.[6] Long-term follow-up of some of the first women to receive a midurethral sling (>17 years ago) suggests that patients have excellent results and minimal complications.[7]

However, in recent years, significant concerns have been raised about the safety of vaginal mesh (used for procedures to treat SUI and pelvic organ prolapse).[8] Several case series have suggested that mesh-based SUI procedures can lead to chronic pain,[9] urethral fistula,[10] significant voiding dysfunction,[11] and mesh erosions into the urethra or the vagina.[6] The treatment of these complications may require surgical revision or removal of the mesh and can leave the patient with substantial residual symptoms and emotional distress.[8,12] In the United States, more than 50 000 women have joined class action lawsuits for transvaginal mesh complications resulting from SUI and prolapse procedures.[13]

The US Food and Drug Administration (FDA)[14] and Health Canada[15] have released warnings stating that complications caused by vaginal mesh are not uncommon, that surgeons should obtain specialized training in their use, and that the risk factors for complications have not been well identified. In light of these statements, we conducted a population-based cohort study with the following objectives: (1) to measure the incidence of mesh removal or revision after a mesh sling procedure for SUI, (2) to assess the potential effect of surgeon volume and specialty, and (3) to determine whether specific risk factors exist for mesh removal or revision.

Methods

Study Design and Setting

We conducted this study through the Institute for Clinical Evaluative Sciences according to a prespecified protocol. This study was approved by the research ethics board at Sunnybrook Hospital, Toronto, Ontario, Canada. Individual patient consent was waived by the research ethics board, in keeping with provincial privacy regulations. All data were deidentified.

We performed a population-based, retrospective cohort study of all adult women who underwent a mesh sling implant for SUI from April 1, 2002, through December 31, 2012, in the province of Ontario (which has a population of approximately 13 million people, all of whom have unlimited access to a single universal health care system). The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines were followed (eTable 1 in the Supplement).[16]

Data Sources

Our study population, outcomes, exposures, and covariates were obtained using 3 linked databases. The Discharge Abstract and Same Day Surgery databases of the Canadian Institute for Health Information (CIHI-DAD/SDS) capture all diagnostic and procedural information for patients in Ontario who have a hospital admission or a surgical procedure (inpatient and outpatient). The Ontario Health Insurance Plan database captures all health claims for inpatient and outpatient care rendered by physicians. Finally, the Registered Persons Database contains demographic information on all individuals in Ontario. The databases are considered complete for all study variables, aside from physician specialty, which was unknown for 150 of 1068 of relevant physicians (14.0%). All databases have patient-level data available from October 1, 1992, through March 31, 2013. The accuracy of these databases has been previously measured,[17-19] and data elements are valid and reliable.

Patient Population

Canadian Classification of Health Intervention (CCI) codes from the CIHI-DAD/SDS database were used to identify our cohort of adult women who underwent a mesh-based surgical procedure for SUI during our study period (eTable 2 in the Supplement). The date of the procedure was considered the index date, and patients were followed up until death, emigration from the province, the first occurrence of an outcome, or the end of the study (March 31, 2013). We excluded women who may have had a mesh-based procedure for SUI before April 1, 2002 (n = 56), and women who had a mesh-based procedure for pelvic organ prolapse before or during our study period (n = 1101) (eFigure 1 in the Supplement).

Outcome

We used CCI codes to identify our composite outcome of the first reoperation for SUI mesh-related complications (eTable 3 in the Supplement). We included specific codes related to the surgical removal or revision of vaginal or urethral mesh or removal of a foreign body, endoscopic treatment of a urethral foreign body or mesh encrustation, urethrolysis, or repair of a urethrovaginal fistula. Rare acute surgical complications of SUI mesh procedures, such as adjacent organ or major-vessel injury, hematoma, and necrotizing infections, have been characterized previously[11] and were not included in this study.

Exposures and Covariates

We prespecified surgeon volume and specialty as the primary exposures of interest, with a hypothesized inverse relationship between volume and complications and a hypothesized difference in the complication rate between urologists and gynecologists. *Surgeon volume* was defined as the number of mesh-based procedures for SUI performed per year and was

determined using unique physician identifiers in the CIHI-DAD/SDS database. *High-volume surgeons* were defined as being at the 75th percentile or greater for mesh implants for SUI in a given year, and surgeons could move between high- and low-volume categories with each successive year. Surgeon specialty was classified as urology, obstetrics/gynecology, or undetermined using the CIHI-DAD/SDS database. Secondary exposures included patients at high risk for mesh-related complications (a binary variable indicating a previous urinary fistula, urethral diverticulum, urethral injury, or pelvic radiotherapy[20,21]) and those with multiple mesh slings. Other covariates (eTable 4 in the Supplement) were age, obesity (body mass index [calculated as weight in kilograms divided by height in meters squared] >40), diabetes mellitus,[22] combined hysterectomy or non-mesh-based repair of pelvic organ prolapse, provincial region, academic or community hospital, rural residence,[23] general medical comorbidity (health care usage served as a proxy for overall health and was determined from the Aggregated Diagnostic Groups resource utilization bands from the validated Johns Hopkins University Adjusted Case Groups case-mix system[24,25]), socioeconomic status (using the Ontario Marginalization Index, a measure of regional marginalization, which served as a proxy for individual socioeconomic status[26]), and health care usage in the year before the mesh-based procedure for SUI.

Statistical Analysis

Data analysis was performed from November 1, 2014, through February 28, 2015. All baseline characteristics are reported as frequencies (number [percentage]) or medians (interquartile range [IQR]). We compared patient baseline characteristics between high- and low-volume surgeons using standardized differences.[27] This method identifies clinically meaningful differences (standardized difference, >10%) as opposed to statistically significant differences (which are likely with large sample sizes).[27]

Our primary analysis was a multivariable survival analysis performed using the PROC PHREG procedure in SAS software (version 9.3; SAS Institute Inc). Results are reported as hazard ratios (HRs) with 95% CIs and *P* values ($P < .05$ was considered significant). We included surgeon volume and specialty, high-risk patients, and the number of mesh slings (modeled as a time-varying covariate to account for different periods during which the patient would be at risk owing to an increasing number of consecutive procedures). We adjusted for age, obesity, diabetes mellitus, other pelvic surgery, Aggregated Diagnostic Groups resource utilization bands (as an ordinal variable), provincial region, hospital type, rurality, and socioeconomic status. The Cochrane-Armitage test for linear trends[28] was used to assess for significant changes in the 1-year event rate over time.

A number of post hoc sensitivity analyses were performed to confirm the effects of our primary and secondary exposures. First, we restricted the patient population to those with CCI codes suggesting a midurethral sling implant (as opposed to other potential mesh-based surgical procedures for SUI, such as bladder-neck mesh sling implants). Second, we censored patients on future non-mesh-based SUI surgery. Third, we varied our definition of high-volume surgeon to those who performed procedures at the 50th percentile or greater among all surgeons performing the mesh-based procedures in a given year. Fourth, we explored the volume outcome relationship graphically. Fifth, we considered multiple mesh slings as a count variable. Finally, we accounted for patient clustering within individual surgeons using a hierarchical model.

Results

Baseline Characteristics

We identified 59 887 women who underwent mesh-based procedures for SUI during the study period. Median follow-up was 4.4 (IQR, 2.4-6.9) years. One thousand seven hundred forty women (2.9%) were censored for death; 915 women (1.5%), for emigration.

The surgical procedures were performed by 1068 unique surgeons (293 urologists [27.4%], 625 gynecologists [58.5%], and 150 unspecified [14.0%]). The overall number of procedures increased from 2002 through 2009 and then declined (eFigure 2 in the Supplement). The numbers of high- and low-volume surgeons are shown in eFigure 3 in the Supplement. Patients were classified as having received a sling from a high-volume surgeon (≥75th percentile for the yearly volume of surgeons performing mesh-based procedures for SUI) or a low-volume surgeon (<75th percentile), and the baseline characteristics of our cohort are shown in **Table 1**. The median cutoff for the number of yearly mesh-based procedures for SUI that defined high-volume surgeons during each year of the 10-year study was greater than 16 (IQR, 13-18). High-volume surgeons were less likely to perform a simultaneous hysterectomy (11.5% vs 16.5%; standardized difference, 0.14), were more likely to perform surgery in an academic center (28.9% vs 16.3%; standardized difference, 0.30), and saw the patient less frequently in the year before the surgery (median, 2 [IQR, 1-3] vs 3 [IQR, 2-4] visits; standardized difference, 0.26). We found significant regional variation, with patients in some regions being more or less likely to be treated by a low-volume surgeon.

Primary Analysis

Overall, 1307 women (2.2%) underwent mesh removal or revision a median of 0.94 (IQR, 0.35-2.49) years after receiving a mesh implant for SUI (**Table 2**). The sling complication was treated by the same surgeon responsible for the original procedure in 812 of the 1307 cases (62.1%). The cumulative incidence rate of the complications of interest increased from 1.17 (95% CI, 1.09-1.27) at 1 year to 3.29 (95% CI, 3.05-3.53) at 10 years (**Table 3**). Unadjusted analysis demonstrated that patients of low-volume surgeons had a 37% (95% CI, 17%-49% [$P < .01$]) higher relative risk and a 0.63% (95% CI, 0.36%-0.92%) increased absolute risk for mesh removal or revision compared with patients treated by high-volume surgeons (HR, 0.73 [0.65-0.83]); the effect of surgical specialty was not significant. Similarly, in our multivariable model,

Table 1. Baseline Characteristics of Patients by Surgeon Volume

	Patient Data[a]		Standardized Difference of the Mean[c]
	High-Volume Surgeon[b] (n = 44 140)	Low-Volume Surgeon (n = 15 747)	
Age, median (IQR), y	53 (45-63)	52 (45-63)	0.02
ADG resource utilization band, median (IQR)[d]	3 (3-4)	4 (3-4)	0.06
BMI >40 (obese)	1976 (4.5)	698 (4.4)	0
Diabetes mellitus	5222 (11.8)	2036 (12.9)	0.03
Simultaneous hysterectomy	5061 (11.5)	2603 (16.5)	0.14
Prior hysterectomy	3633 (8.2)	1329 (8.4)	0.01
Simultaneous non-mesh-based surgery for pelvic organ prolapse	13 115 (29.7)	4743 (30.1)	0.01
Prior non-mesh-based surgery for pelvic organ prolapse	2386 (5.4)	805 (5.1)	0.01
>1 Mesh-based procedure for SUI during the study period	900 (2.0)	352 (2.2)	0.01
High-risk patient[e]	54 (0.1)	19 (0.1)	0
Fiscal year of cohort entry (index date)			
2002[f]	1917 (4.3)	668 (4.2)	0
2003	2664 (6.0)	859 (5.5)	0.02
2004	3199 (7.2)	1005 (6.4)	0.03
2005	4056 (9.2)	1251 (7.9)	0.05
2006	4144 (9.4)	1584 (10.1)	0.02
2007	4727 (10.7)	1669 (10.6)	0
2008	5218 (11.8)	1759 (11.2)	0.02
2009	5177 (11.7)	2055 (13.1)	0.04
2010	4836 (11.0)	1859 (11.8)	0.03
2011	4969 (11.3)	1835 (11.7)	0.01
2012[g]	3233 (7.3)	1203 (7.6)	0.01
Patients' provincial region[h]			
1	6175 (14.0)	1461 (9.3)	0.15
2	4081 (9.2)	1466 (9.3)	0
3	1312 (3.0)	241 (1.5)	0.10
4	3972 (9.0)	899 (5.7)	0.13
5	5610 (12.7)	2233 (14.2)	0.04
6	1855 (4.2)	830 (5.3)	0.05
7	2436 (5.5)	949 (6.0)	0.02
8	1191 (2.7)	692 (4.4)	0.09
9	2806 (6.4)	1557 (9.9)	0.13
10	3093 (7.0)	1397 (8.9)	0.07
11	906 (2.1)	932 (5.9)	0.19
12	4548 (10.3)	1105 (7.0)	0.12
13	3522 (8.0)	777 (4.9)	0.13
14	2621 (5.9)	1202 (7.6)	0.07
Ontario Marginalization Index, median (IQR)[i]			
Dependency	3 (2-4)	3 (2-4)	0.04
Material deprivation	2 (1-4)	3 (2-4)	0.10
Ethnic concentration	3 (2-4)	3 (2-4)	0.06
Residential instability	2 (1-4)	3 (2-4)	0.06
Rural residence	8290 (18.8)	3025 (19.2)	0.01
Surgeon specialty			
Urology	18 946 (42.9)	6648 (42.2)	0.01
Obstetrics/gynecology	25 133 (56.9)	8837 (56.1)	0.02
Unknown	61 (0.1)	262 (1.7)	0.17
Teaching or academic hospital	12 762 (28.9)	2562 (16.3)	0.30

(continued)

Table 1. Baseline Characteristics of Patients by Surgeon Volume (continued)

	Patient Data[a]		Standardized Difference of the Mean[c]
	High-Volume Surgeon[b] (n = 44 140)	Low-Volume Surgeon (n = 15 747)	
No. of health care resources used 1 y before mesh-based procedure for SUI, median (IQR)			
Family physician visits	6 (3-9)	6 (3-9)	0.05
Urology or gynecology visits	2 (1-3)	3 (2-4)	0.26
Hospital admissions	0 (0-0)	0 (0-0)	0.04
Death after index event	1289 (2.9)	485 (3.1)	0.01
Emigration	683 (1.5)	232 (1.5)	0

Abbreviations: ADG, Aggregated Diagnostic Groups; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range; SUI, stress urinary incontinence.

[a] A *high-volume surgeon* is defined as being at the 75th percentile or higher for mesh implants for SUI in a given year; a *low-volume surgeon*, at less than the 75th percentile. Unless otherwise indicated, data are expressed as the number (percentage) of patients. Percentages have been rounded and may not total 100.

[b] Indicates 75th percentile or higher for procedures performed for SUI.

[c] Standardized differences of the mean are less sensitive to sample size than traditional hypothesis testing. A value of greater than 10% (0.1) is considered a meaningful difference between groups.

[d] Using the ADG codes, we assigned 1 of 6 resource utilization bands to patients based on their health care usage and the severity and chronicity of the medical problems for which they access health care services (0 indicates nonusers; 1, healthy users; 2, low morbidity; 3, moderate morbidity; 4, high morbidity; and 5, very high morbidity). This claims-based comorbidity adjustment system considers inpatient and outpatient care and categorizes comorbidities based on the duration, severity, and cause of the comorbidity. This system better discriminates the comorbidities of a patient population that rarely received inpatient care.

[e] Includes history of fistula, diverticulum, radiotherapy, or urethral injury.

[f] Indicates April 1, 2002, through March 30, 2003.

[g] Indicates April 1 through December 30, 2012.

[h] The province of Ontario is separated into 14 local health integration networks, based on geographic boundaries, which are responsible for planning, integrating, and funding local health care. These regions were anonymized according to privacy regulations. This information was missing for 12 patients in the high-volume surgeon category and 6 patients in the low-volume surgeon category (standardized difference, 0).

[i] The Ontario Marginalization Index[26] is a geographically based, multidimensional index derived from Canadian Census data that is used as a proxy for individual marginalization (1 indicates least marginalized; 5, most marginalized). These domains assess 18 different socioeconomic and marginalization variables for small geographic areas, such as the proportion of people older than 65 years or younger than 14 years (dependency), proportion unemployed (material deprivation), proportion of visible minorities (ethnic concentration), and proportion of dwellings not owned (residential instability).

Table 2. Mesh Revision and Removal After Placement of a Synthetic Sling for SUI

		Surgeon Volume[a]		Surgical Specialty[b]	
	Entire Cohort (N = 59 887)	High (n = 44 140)	Low (n = 15 747)	Urology (n = 25 594)	Gynecology (n = 33 970)
Duration of follow-up, median, (IQR), y	4.43 (2.35-6.88)	4.50 (2.38-6.96)	4.24 (2.24-6.68)	4.96 (2.68-7.46)	4.10 (2.13-6.38)
Total follow-up, person-years	282 801	210 483	72 318	131 036	150 074
Events, No. (%) of patients	1307 (2.2)	890 (2.0)	417 (2.6)	584 (2.3)	712 (2.1)
Time from index date to outcome, median (IQR), y	0.94 (0.35-2.49)	0.94 (0.34-2.59)	0.93 (0.35-2.38)	1.00 (0.32-2.83)	0.90 (0.37-2.23)
Event rate per 1000 patient-years of follow-up (95% CI)	4.62 (4.38-4.88)	4.23 (3.96-4.52)	5.77 (5.24-6.35)	4.46 (4.11-4.83)	4.74 (4.41-5.11)
Unadjusted risk ratio (95% CI)		1 [Reference]	1.37 (1.17-1.49)[c]	1 [Reference]	0.92 (0.82-1.02)[d]

Abbreviations: IQR, interquartile range; SUI, stress urinary incontinence.

[a] Defined in Table 1.

[b] Three hundred twenty-three patients underwent operations from 1 of 150 surgeons with an unknown surgical specialty.

[c] $P < .01$ compared with a high surgeon volume.

[d] $P = .13$ compared with a urologist.

patients of low-volume surgeons were significantly more likely to experience the composite outcome (HR, 1.37 [95% CI, 1.21-1.55]; $P < .01$), and the difference between surgical disciplines was not significant (**Table 4**).

For our secondary exposures, 1252 women (2.1%) had multiple mesh sling implants (of whom 1191 [95.1%] had 2 and 61 [4.9%] had ≥3), and 73 women (0.1%) had potential risk factors for mesh-related complications. Among women with multiple mesh-based procedures for SUI, the absolute risk for mesh removal or revision was 4.87% (95% CI, 3.86%-6.06%). In multivariable modeling, these women had a 4.73-fold increased hazard of this complication (95% CI, 3.62-6.17 [$P < .01$]) and an absolute risk increase of 2.8% (95% CI, 1.7%-4.1%). The HR among women who had risk factors for mesh removal or revision was not significant (0.58 [95% CI, 0.08-4.13; $P = .59$]). The rate of intervention for SUI-related mesh revision or removal during the first postoperative year increased significantly during the study period from 9.74 per 1000 person-years in 2002 to 14.84 per 1000 person-years in 2012 ($P < .001$; eTable 5 in the Supplement).

Table 3. The Cumulative Incidence Rate of Mesh Revision and Removal After Stress Urinary Incontinence Treatment by Years of Follow-up

Year	No. of Patients			Cumulative Incidence (95% CI)
	At the Beginning of Follow-up	Censored	With Mesh Removal or Revision During Follow-up	
1	59 887	4563	681	1.17 (1.09-1.27)
2	54 643	7042	234	1.63 (1.52-1.74)
3	47 367	6795	118	1.90 (1.78-2.02)
4	40 454	7267	83	2.12 (2.00-2.24)
5	33 104	6955	64	2.33 (2.20-2.46)
6	26 085	6210	48	2.54 (2.39-2.69)
7	19 827	5504	28	2.69 (2.53-2.85)
8	14 295	5013	25	2.90 (2.72-3.08)
9	9257	3874	16	3.11 (2.91-3.31)
10	5367	3134	7	3.29 (3.05-3.53)

Sensitivity Analysis

The results of the sensitivity analyses are described in eTable 6 in the Supplement. The statistical significance and direction of effect for our primary and secondary exposures across all of these analyses were consistent. The probability of experiencing an SUI-related mesh complication based on the surgeon's annual procedure volume is shown in the **Figure**.

Discussion

Mesh-based slings are appropriate for most female patients with SUI.[29,30] For women with complications, surgical intervention is considered the standard of care for mesh erosions into the urinary tract or urinary fistula and for most women with vaginal mesh exposure, significant voiding dysfunction, or severe pelvic pain after surgery.[6,9-11] Over time, early surgical interventions have become more common (eTable 5 in the Supplement), perhaps as a result of increased patient awareness[31] and improved physician confidence and experience with operative management of mesh complications. We have demonstrated that among our cohort of women undergoing vaginal mesh-based procedures solely for SUI, 2.2% underwent operative intervention for these complications (cumulative incidence rate, 3.29 at 10 years). Our results are consistent with an analysis of data from US health maintenance organizations[32] that reported a 9-year rate of urethrolysis or mesh removal of 3.7% and a meta-analysis of clinical trial data[33] that determined an overall proportion of patients requiring any secondary surgery of 3.2%. Although the FDA in the past has treated all vaginal mesh implants as equivalent, the intervention rates for mesh-based complications in procedures for SUI appear to be lower than those associated with procedures for pelvic organ prolapse.[34]

A surgeon volume of mesh-based procedures for SUI of less than the 75th percentile was associated with a 37% increased risk for surgically managed mesh-related complications. Although surgeon volume has been shown to be important for complex operations, such as oncologic and cardiac surgery,[35] its role in less demanding procedures is not well defined. The vaginal mesh regulatory notifications and expert opinion suggest that surgeons should obtain specialized training and experience in vaginal mesh surgery[8,14,15]; the demonstrated volume-outcome relationship (Figure) in this study supports this assertion. Urologists and gynecologists have very different surgical training and day-to-day practices, and previous studies[36] have suggested that differences exist in SUI outcomes between these groups of physicians. We hypothesized that complication rates may differ between these 2 groups; however, our hypothesis was not proved. This finding suggests that procedure-specific knowledge and experience is important for surgery to treat SUI rather than general operative training.

The prospective assessment of risk factors for SUI-related complications of mesh implants requiring surgical intervention is challenging given their rarity and prolonged time to presentation. Registries, such as the FDA Manufacturer and User Facility Device Experience database, and case series have significant reporting bias.[11] However, observational administrative data studies are well suited to address this question. We demonstrated that undergoing 2 or more mesh-based procedures for SUI is associated with an almost 5-fold increased risk for complications. This novel finding should temper the enthusiasm of case series that suggest that the use of multiple synthetic slings is safe and efficacious.[37,38] This finding is particularly important because undergoing additional mesh-based sling implant procedures (presumably for recurrent SUI) is the primary practice pattern in our cohort (and others[39]): after an initial mesh sling implant, and before surgery for a mesh-related complication, 1307 women underwent an additional mesh sling implant procedure, whereas only 147 women underwent a secondary non-mesh-based procedure for SUI. We did not demonstrate a significant increased risk among women who are considered to be at higher risk for complications from a mesh-based procedure for SUI.[20] This finding is likely a result of the very small number of these patients within our cohort, which in itself is reassuring in terms of patient selection.

The other covariates in our study also deserve discussion. Being younger was associated with a higher likelihood of mesh removal or revision, possibly as a result of more aggressive surgical management of complications[32] and an

Table 4. Multivariable Survival Analysis to Assess Independent Patient and Surgeon Risk Factors Associated With Mesh-Related Complication After Procedure for SUI

Variable	HR (95% CI)	*P* Value
Surgeon volume[a]		
High	1 [Reference]	
Low	1.37 (1.21-1.55)	<.01
Surgeon specialty		
Urology	1 [Reference]	NA
Gynecology	0.94 (0.83-1.08)	.38
Unknown	1.18 (0.64-2.17)	.59
Multiple mesh-based procedures for SUI	4.73 (3.62-6.17)	<.01
High-risk patient[b]	0.58 (0.08-4.13)	.59
Age per 10-y increase	0.86 (0.82-0.90)	<.01
ADG resource utilization band[c]	1.31 (1.21-1.41)	<.01
Obesity	0.82 (0.62-1.10)	.19
Diabetes mellitus	1.11 (0.94-1.32)	.22
Simultaneous hysterectomy	1.24 (1.08-1.42)	<.01
Simultaneous non-mesh-based surgery for pelvic organ prolapse	0.80 (0.66-0.97)	.02
Provincial region[d]		
1	1 [Reference]	
2	1.72 (1.35-2.20)	<.01
3	2.38 (1.71-3.30)	<.01
4	1.66 (1.29-2.14)	<.01
5	1.40 (1.10-1.78)	<.01
6	1.35 (0.99-1.85)	.06
7	1.26 (0.92-1.71)	.15
8	0.85 (0.55-1.31)	.47
9	1.58 (1.21-2.06)	<.01
10	1.11 (0.84-1.47)	.47
11	1.27 (0.87-1.84)	.22
12	1.06 (0.80-1.41)	.67
13	1.19 (0.90-1.58)	.22
14	1.41 (1.06-1.87)	.02
Ontario Marginalization Index[d]		
Dependency	1.02 (0.97-1.07)	.46
Deprivation	1.01 (0.96-1.06)	.70
Ethnic concentration	0.99 (0.94-1.04)	.65
Instability	0.99 (0.94-1.04)	.73
Academic or teaching hospital	1.18 (1.02-1.36)	.03

Abbreviations: ADG, Aggregated Diagnostic Groups; SUI, stress urinary incontinence.

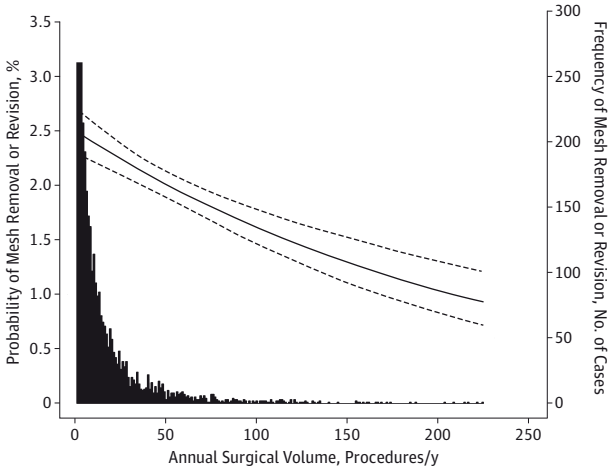
[a] Defined in Table 1.

[b] Includes history of fistula, diverticulum, radiotherapy, or urethral injury.

[c] Defined in Table 1. The reference category is band 0/1, indicating a healthy user.

[d] Defined in Table 1.

Figure. Predicted Probability of Mesh-Related Complication in the Treatment of Stress Urinary Incontinence by Annual Surgeon Volume



The overlying histogram plot shows the distribution of annual surgeon volume. Predicted probability (solid line) was calculated using a logistic regression model with the same covariates as the primary analysis and was based on the observed sample means and proportions for each of the covariates. Dashed lines represent the 95% CI.

increased likelihood of dyspareunia. Increased comorbidity was associated with increased mesh removal or revision, which may be caused by impaired healing and preexisting voiding dysfunction from concurrent medical conditions. The additional dissection, trauma to the pelvic nerve plexus, and postoperative change to the vaginal anatomy may account for the increased risk for complications observed with a simultaneous hysterectomy and mesh-based procedure for SUI.[32,34] The increased risk for mesh removal or revision associated with academic hospitals may be owing to an increased clinical vigilance for complications or to unadjusted case-mix differences compared with nonacademic hospitals. The involvement of surgical trainees may also play a role because an increased risk for morbidity with trainee involvement has been demonstrated across a large spectrum of surgical procedures[40] and specifically among urology residents performing urogynecologic procedures.[41] The reduced risk observed with simultaneous prolapse surgery may be a marker of more favorable vagina exposure at the time of sling placement. The significant regional variation across Ontario (despite multivariable adjustment) may be owing to regional preferences for specific commercial mesh slings, different training and mentoring for practicing surgeons learning the procedure, and varying access to tertiary referral practices for complex issues, such as pain or voiding dysfunction after mesh sling procedures.

Our study has several strengths. This population-based study addresses multiple key questions from the FDA and Health Canada and substantiates their recommendation that surgeons should obtain training and experience in the use of vaginal mesh implants for SUI. Ontario's health care databases and universal health care system provide a large and inclusive population of women treated by a variety of surgeons and with a variety of mesh types and mesh-based procedures. This setting maximizes the precision and generalizability of our results compared with the results of randomized clinical trials that rely on highly selected patients treated at specialist centers. Across several sensitivity analyses, the magnitude and significance of our primary and secondary exposures were consistent.

The limitations of this study should also be acknowledged. Despite measuring several important covariates, observational studies may have residual confounding; for example, the degree of incontinence, smoking status, and type of mesh could not be measured. Although the CCI codes as a whole defined our cohort and primary outcome well, we could not reliably identify specific sling types (such as retropubic or transobturator slings or mini-slings) or specific complications. Some outcomes in our study may not have had a direct causal link with the mesh-based procedure for SUI. Finally, we relied on surgical removal or revision of mesh as our outcome. This measure captures the most serious complications; however, we have likely underestimated the true absolute rate of mesh-related complications because we were not able to include asymptomatic patients, those with nonsurgical complications, or those treated outside the operating room.

Conclusions

Among adult women undergoing mesh-based procedures for SUI, the risk for secondary surgery for specific complications is low (cumulative incidence rate, 3.29 at 10 years). Patients of lower-volume surgeons are 37% more likely to require surgery for mesh complications. These findings support the regulatory statements that suggest that patients should be counseled regarding serious complications that can occur with mesh-based procedures for SUI and that surgeons should achieve expertise in their chosen procedure. Multiple mesh-based procedures for SUI are a novel risk factor associated with an almost 5-fold higher rate of mesh removal or revision, and the safety of this practice should be studied further.

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Study concept and design: Welk.
Acquisition, analysis, or interpretation of data: All authors.
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Critical revision of the manuscript for important intellectual content: All authors.
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Supplemental Online Content

Welk B, Al-Hothi H, Winick-Ng J. Removal or revision of vaginal mesh used for the treatment of stress urinary incontinence. *JAMA Surg*. Published online September 9, 2015. doi:10.1001/jamasurg.2015.2590

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. STROBE Checklist for Cohort Studies

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Abstract, *Design*
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction
Objectives	3	State specific objectives, including any prespecified hypotheses	Introduction & Methods
Methods			
Study design	4	Present key elements of study design early in the paper	Methods, *Study Design & Setting*
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods, *Study Design & Setting* and *Primary Exposure*
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Methods
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Methods, *Outcome* and *Exposures and covariates*
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Methods, *Data sources* and Table 1, and eTable2-4 in the Supplement.
Bias	9	Describe any efforts to address potential sources of bias	Methods, *Statistical analysis*
Study size	10	Explain how the study size was arrived at	Methods, eFigure 1, population based study
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods, *Exposures and covariates* and *Statistical analysis* and Table 1. Additional information: The exposure (surgeon volume >75th percentile was based on previous studies in the literature, and the robustness of this definition was tested

			with an alternative definition (50^{th} percentile), and graphical assessment (Figure 1). Other variables: age (continuous), ADG RUB (continuous), obesity (binary), hysterectomy (binary), prior prolapse surgery (binary), multiple mesh slings (binary, sensitivity analysis as count variable), high risk patient (Binary variable), Year of cohort entry (categorical), provincial region (categorical), Ontario Marginalisation index domains (continuous), rural residence (binary), surgeon (categorical), teaching hospital (binary), Health care utilisation (continuous).
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Methods, *Statistical analysis*
		(*b*) Describe any methods used to examine subgroups and interactions	None
		(*c*) Explain how missing data were addressed	Methods, *Data sources*
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	Methods Patients were censored on death or emigration (date of last healthcare contact plus one year)
		(*e*) Describe any sensitivity analyses	Methods, *Statistical analysis*
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	eFigure 1 in the supplement
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	eFigure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Results, Table 1, Table 2
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Table 2
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures	Table 2

		over time	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Results, Table 2, Table 4
		(*b*) Report category boundaries when continuous variables were categorized	Results Interquartile range
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Results Included for the significant exposures of high volume surgeon and multiple mesh slings
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	eTable 6 in the supplement
Discussion			
Key results	18	Summarise key results with reference to study objectives	Discussion
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Discussion
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion
Generalisability	21	Discuss the generalisability (external validity) of the study results	Discussion
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Acknowledgements

eTable 2. CCI Codes Used to Identify Any Synthetic Mesh-Based Procedure for SUI

CCI Code	Dates Active	Description	Number of patients in cohort
1PL74AFFF	April 2002-March 2006	Fixation, bladder neck combined open abdominal and endoscopic transvaginal approach using tension free vaginal tape [TVT] technique	2913
1PL74AFXXN	April 2002-Present	'Fixation, bladder neck combined per orifice (vaginal) and open (abdominal) approach using synthetic material	3677
1PL74AFXXQ	April 2003-Present	'Fixation, bladder neck combined per orifice (vaginal) and open (abdominal) approach using combined sources of tissue [e.g. graft and synthetic tissue]	66
1PL74ALFF	April 2002-March 2006	'Fixation, bladder neck combined percutaneous and vaginal approach using tension free vaginal tape [TVT] technique	11535
1PL74ALXXN	April 2006-Present	Fixation, bladder neck combined per orifice (vaginal) and percutaneous approach using synthetic material (e.g. TVT technique)	32268
1PL74CRXXN	April 2009-Present	'Fixation, bladder neck per orifice (vaginal) approach with incision using synthetic tissue (e.g. TVT technique)	7932
1PL74DAXXN	April 2009-Present	'Fixation, bladder neck endoscopic (laparoscopic) (retropubic) approach using synthetic tissue	549
1PL74LAXXN	April 2006-Present	Fixation, bladder neck open (retropubic, perineal) approach using synthetic material (sling)	933
1PL74LAXXQ	April 2006-Present	Fixation, bladder neck open (retropubic, perineal) approach using combined sources	14

Codes were selected after review of CIHI CCI code description/evolution guides, yearly coding frequency, and review of actual coding practices with trained hospital based CIHI coders. Other distinct CCI codes specify alternative slings, such as biologic graft and autologous fascial slings.

eTable 3. CCI Codes Used to Define Our Composite Outcome of Mesh Removal or Revision

CCI Code	Dates Active	Description	Count*
1PL54CAXXN	April 2006-Present	Management of internal device, bladder neck of synthetic urethral sling (tension free vaginal tape [TVT]) using per orifice [vaginal] approach	248
1PL54LAXXN	April 2006-Present	Management of internal device, bladder neck of synthetic material (urethral sling) (tension free vaginal tape [TVT]) using open approach	67
1PL55CAXXN	April 2006-Present	Removal of device, bladder neck of synthetic urethral sling [tension free vaginal tape] using vaginal approach	393
1PL55LAXXN	April 2006-Present	Removal of device, bladder neck of synthetic urethral sling [tension free vaginal tape] using open approach	86
1PQ56BA	April 2002-Present	Removal of foreign body, urethra using endoscopic per orifice (transurethral) approach	26
1PQ56CA	April 2002-Present	Removal of foreign body, urethra using per orifice approach	7
1PQ56DA	April 2002-Present	Removal of foreign body, urethra using endoscopic (percutaneous) approach	0
1PQ56LA	April 2002-Present	Removal of foreign body, urethra using open approach (abdominal, perineal)	<6
1PQ56QY	April 2002-Present	Removal of foreign body, urethra using open transvaginal approach	10
1PQ57BAGX	April 2002-Present	Extraction, urethra using endoscopic per orifice approach(transurethral) and device NEC [e.g. forceps, meatome]	<6
1PQ57LAAM	April 2002-Present	Extraction, urethra using open approach and basket device	0
1PQ57LAGX	April 2002-Present	Extraction, urethra using open approach and device NEC [e.g. forceps, meatome]	<6
1PQ59BAAG	April 2002-Present	Destruction, urethra endoscopic per orifice approach using laser	10
1PQ59BAAZ	April 2002-Present	Destruction, urethra endoscopic per orifice approach using ultrasonic probe	0
1PQ72AC	April 2002-Present	Release, urethra using combined open abdominal with vaginal approach	27
1PQ72LA	April 2002-Present	Release, urethra using open approach	49
1PQ72PK	April 2002-Present	Release, urethra using open retropubic approach	8
1PQ72QY	April 2009-Present	Release, urethra using open transvaginal approach	42
1PQ72QYAG	April 2002-Present	Release, urethra using open transvaginal approach and laser	11
1PQ86MB	April 2002-Present	Closure of fistula, urethra simple excision and closure terminating at skin (urethrocutaneous, urethroscrotal, urethroperineal)	0
1PQ86MD	April 2002-March 2009	Closure of fistula, urethra NEC simple excision and closure terminating in genital tract [urethrovaginal]	10
1PQ86MH**	April 2009-Present	Closure of fistula, urethra simple excision and closure terminating in genital tract [urethrovaginal]	<6

1RS55CAXXN	April 2003-Present	Removal of device, vagina of synthetic material (e.g. mesh, sling) using per orifice approach	256
1RS55LAXXN	April 2002-Present	Removal of device, vagina of synthetic tissue (e.g. mesh) using open approach	65
1RS56CA	April 2002-Present	Removal of foreign body, vagina using per orifice [vaginal] approach (for simple extraction)	18
1RS56CR	April 2002-Present	Removal of foreign body, vagina using per orifice [vaginal] approach and incisional technique	65
1RS56DA	April 2006-Present	Removal of foreign body, vagina using endoscopic (laparoscopic) approach	<6
1RS56LA	April 2006-Present	Removal of foreign body, vagina using open (abdominal) approach	<6
1RS86LAXXE	April 2002-March 2006	Closure of fistula, vagina NEC terminating at skin, using open (perineal) approach and local flap repair	<6
1RS86MB	April 2006-Present	Closure of fistula, vagina for fistula terminating at skin (vaginal, perineal) and simple apposition (suturing) for closure	<6
1SZ55LAXXN	April 2002-Present	Removal of device, soft tissue of the chest and abdomen of mesh using open approach	91

Codes were selected after review of CIHI CCI code description/evolution guides, yearly coding frequency, and review of actual coding practices with trained hospital based CIHI coders. Due to the procedure based rather than indication based nature of these codes, and the fact that multiple codes may be assigned to a single surgery, we could not definitively determine the specific reason why most patients were having the mesh removed or revised.

*The number of codes (1509) is greater than the number of patients who experienced an outcome (1307) as patients could have multiple relevant codes for an individual surgery. Groups of patients with n<6 are not reported for privacy reasons.

eTable 4. Coding Definitions for Study Covariates

Covariate	Source	Codes
Obesity	OHIP	E676, E010
	CIHI-DAD/SDS (ICD 10)	E66x Obesity
	CIHI-DAD/SDS (ICD 9)	278.x Obesity
Pelvic organ prolapse repair (with or without mesh)	CIHI-DAD/SDS (CCP*)	82.40 Anterior & Posterior repair 82.41 Anterior repair 82.42 Posterior repair 82.43 Anterior & Posterior Repair 81.30 Repair of uterine support 81.31 Interposition 81.32 Other uterine suspension 81.33 Vaginal repair chronic uterine inversion 81.39 Other repair of uterine support
Pelvic organ prolapse repair (with mesh)	CIHI-DAD/SDS (CCI)	1RS80CRXXN Synthetic repair vagina (Vaginal approach) 1RS80CAXXN Synthetic repair vagina 1RS80LAXXN Synthetic repair vagina, (abdominal approach) 1RS80DAXXN Synthetic repair vagina (MIS approach) 1RS80CRXXQ Repair vagina combined source 1RS80CAXXQ Repair vagina combined source 1RS80LAXXQ Repair vagina retropubic combined tissue source 1RS74CRXXN Repair vagina with synthetics 1RS74LAXXN Abdominal repair vagina with synthetics 1RS74DAXXN Repair vagina synthetics Lap 1RS74CAXXN Fixation vaginal approach with mesh
Any prolapse repair	OHIP	S716 S717 S718 S719 S723 S720 S721 S722 S812 S760 S813 S761 S758 S759
	CIHI-DAD/SDS (CCI)	1RS74 Fixation vagina 1RS80 Repair vagina
	CIHI-DAD/SDS (CCP)	82.40 Anterior & Posterior repair 82.41 Anterior repair 82.42 Posterior repair 82.43 Anterior & Posterior Repair 81.30 Repair of uterine support 81.31 Interposition 81.32 Other uterine suspension 81.33 Vaginal repair chronic uterine inversion 81.39 Other repair of uterine support
Prior possible mesh based SUI procedure	CIHI-DAD/SDS (CCP)	71.40 Suprapubic sling operation 71.60 Periurethral suspension and compression
Urologic visit	OHIP	A355, C355, W355, A356, C356, W356, A353, C353, C354, A354
Gynecologic visit	OHIP	A205 A206 A203 A204 C205 C206 C203 C204 W305 W306
Hysterectomy	OHIP	S757 S816 S763 S762 S710 S758 S759
	CIHI-DAD/SDS (CCI)	5CA89CK Vaginal Hysterectomy with pregnancy 5CA89GB MIS hysterectomy with pregnancy 5CA89WJ Open hysterectomy with pregnancy 5CA89WK Open hysterectomy with pregnancy 5MD60KE Cesarean section hysterectomy 5MD60RC Cesarean section hysterectomy with forceps 5MD60RD Cesarean section hysterectomy with vacuum

		1RM89 Total hysterectomy
		1RM91 Radical hysterectomy
	CIHI-DAD/SDS (CCP)	86.42 Hysterectomy with pregnancy
		80.30 Total abdominal hysterectomy
		80.40 Vaginal hysterectomy
		80.50 Radical hysterectomy
		80.60 Radical vaginal hysterectomy
High risk mesh patient: Prior fistula	CIHI-DAD/SDS (CCI)	1PQ86MH Urethrovaginal fistula excision and closure
		1PQ86MD Urethrovaginal fistula excision and closure
		1PQ86MB Urethral fistula excision and closure
		1RS86MB Vaginal fistula closure
		1RS86CAXXE Vaginal fistula closure
		1RS86LAXXE Vaginal fistula closure
	OHIP	S709A, S523A, S524A
	CIHI-DAD/SDS (CCP)	70.33 Closure of fistula to urethra
High risk mesh patient: Prior urethral diverticulum	CIHI-DAD/SDS (CCI)	1PQ87QY Partial excision urethra
	CIHI-DAD/SDS (CCP)	70.20 Excision or destruction of urethral lesion
		82.52 Vaginal reconstruction diverticulum
	OHIP	S541
High risk mesh patient: Prior radiation therapy	CIHI-DAD/SDS (CCI)	1PQ27JA Radiation urethra, external beam
		1PM27JA Radiation bladder, external beam
		1RM26 Radiation uterus, brachytherapy
		1RM27JA Radiation uterus, external beam
		1RZ27JA Radiation female genital tract
		1RN26 Radiation cervix, brachytherapy
		1RN27 Radiation cervix, external beam
		1NQ27JA Radiation rectum, external beam
		1NT26CA/HA/LA Radiation anus, brachytherapy
		1NT27JA Radiation anus, external beam
		1RB27JA Radiation ovary, external beam
		1RS26 Radiation vagina, brachytherapy
		1RS27JA Radiation vagina, external beam
High risk mesh patient: Prior urethral injury	CIHI-DAD/SDS ICD10	S37.3 Injury of urethra
	CIHI-DAD/SDS ICD9	867.0 Injury bladder or urethra
		867.1 Open injury bladder or urethra

The entire data holdings were used as appropriate to determine covariate status.

*Canadian Classification of Diagnostic, Therapeutic and Surgical Procedures (CCP) codes were used prior to April 1 2002 after which they were replaced by CCI codes.

eTable 5. One-Year Rate of Mesh Removal or Revision by Operative Year

	Cohort size	Frequency of outcome	Event rate (per 1000 person-years)*
2002	2585	0.97% (25)	9.74
2003	3523	0.74% (26)	7.43
2004	4204	1.05% (44)	10.55
2005	5307	1.00% (53)	10.06
2006	5728	1.13% (65)	11.44
2007	6396	1.06% (68)	10.71
2008	6977	1.33% (93)	13.45
2009	7232	1.18% (85)	11.86
2010	6695	1.34% (90)	13.58
2011	6804	1.47% (100)	14.84
Entire cohort	55451	1.17% (649)	11.80

*There was a significant linear increase in this rate (p=0.0002).

eTable 6. Summary of Sensitivity Analyses for Primary and Secondary Exposures

	Primary Analysis HR (95% CI)	Cohort restricted to patients receiving a midurethral mesh sling (n=54,648)*	Patients censored for future non mesh SUI surgery (n=147 censored)**	Definition of high volume surgeon ≥50th percentile ***	Multiple mesh surgeries modeled as a count variable****	Multilevel model accounting for patient clustering within surgeons*****
Surgeon Volume (reference=high volume)	1.37 (1.21-1.55) p<0.01	1.42 (1.24-1.61) p<0.01	1.36 (1.20-1.53) p<0.01	1.21 (1.01-1.47) p=0.04	1.37 (1.22-1.55) p<0.01	1.37 (1.17-1.60) p<0.01
Surgeon						
Urologist	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
Gynecologist	0.94 (0.83-1.08) p=0.38	0.90 (0.79-1.04) p=0.15	0.95 (0.84-1.09) p=0.47	0.94 (0.83-1.08) p=0.39	0.95 (0.83-1.08) p=0.42	0.94 (0.77-1.16) p=0.58
Unknown	1.18 (0.64-2.17) p=0.59	0.98 (0.48-1.99) p=0.36	1.21 (0.66-2.22) p=0.54	1.24 (0.67-2.30) p=0.49	1.21 (0.66-2.22) p=0.54	1.18 (0.69-2.03) p=0.55
Multiple mesh based SUI procedures	4.73 (3.62-6.17) p<0.01	5.30 (4.04-6.96) p<0.01	4.71 (3.59-6.18) p<0.01	4.74 (3.63-6.19) p<0.01	3.37 (2.76-4.11) p<0.01	4.73 (3.48-6.42) p<0.01
High risk patient (history of fistula, diverticulum, radiation, urethral injury)	0.58 (0.08-4.13) p=0.59	0.61 (0.09-4.31) p=0.62	0.60 (0.08-4.30) p=0.62	0.57 (0.08-4.06) p=0.58	0.59 (0.08-4.16) p=0.59	0.58 (0.08-4.17) p=0.59

*Cohort was restricted to CCI codes 1PL74AFFF, 1PL74ALFF, 1PL74ALXXN, 1PL74CRXXN, which were most definitively linked to a midurethral sling (tension free vaginal tape placed by either a transvaginal or transobturator technique). Excluded patients may have had bone anchored slings, bladder neck slings placed open or with laparoscopic assistance, or procedures that used combined mesh and biologic implants.

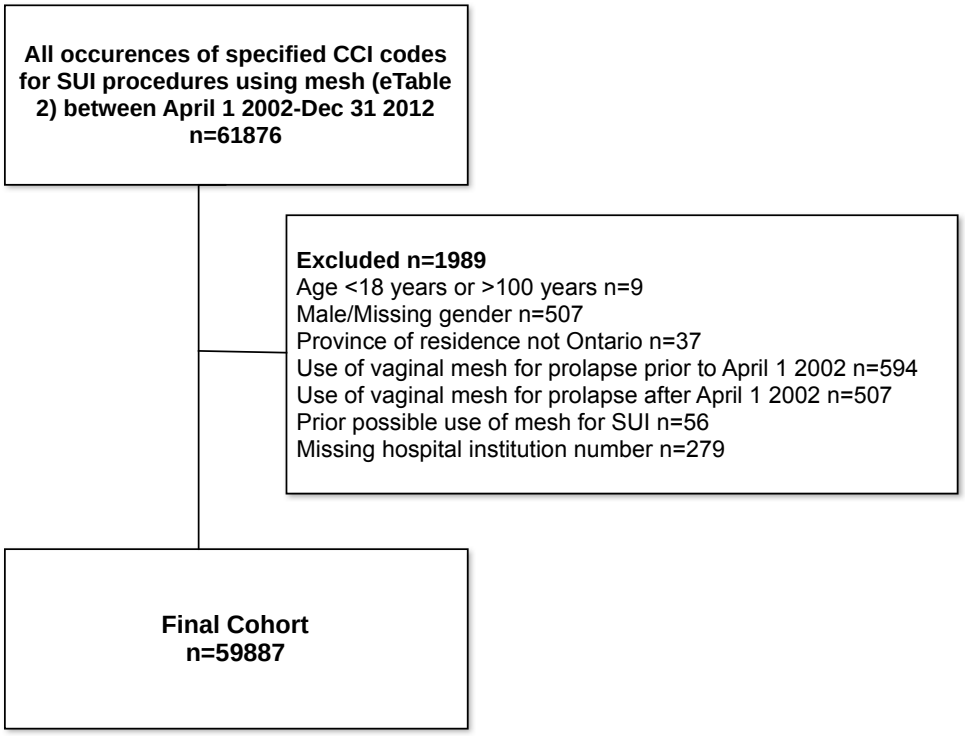
**Patients who had a subsequent retropubic suspension, fascial or biologic bladder neck sling, or bulking agent were censored on the date of this procedure. This removes the potential issue of assigning causality to the initial mesh based SUI procedure when obstruction, mesh exposure or fistula may be due to complications of the subsequent nonmesh procedure.

***To be considered in the top 50th percentile of mesh implanters in a given year, surgeons had a median yearly volume of ≥6 (IQR 4-7) mesh based procedures.

****Rather than defining multiple mesh slings as binary variable, this model's HR for multiple mesh slings is additive for each additional mesh based SUI procedure

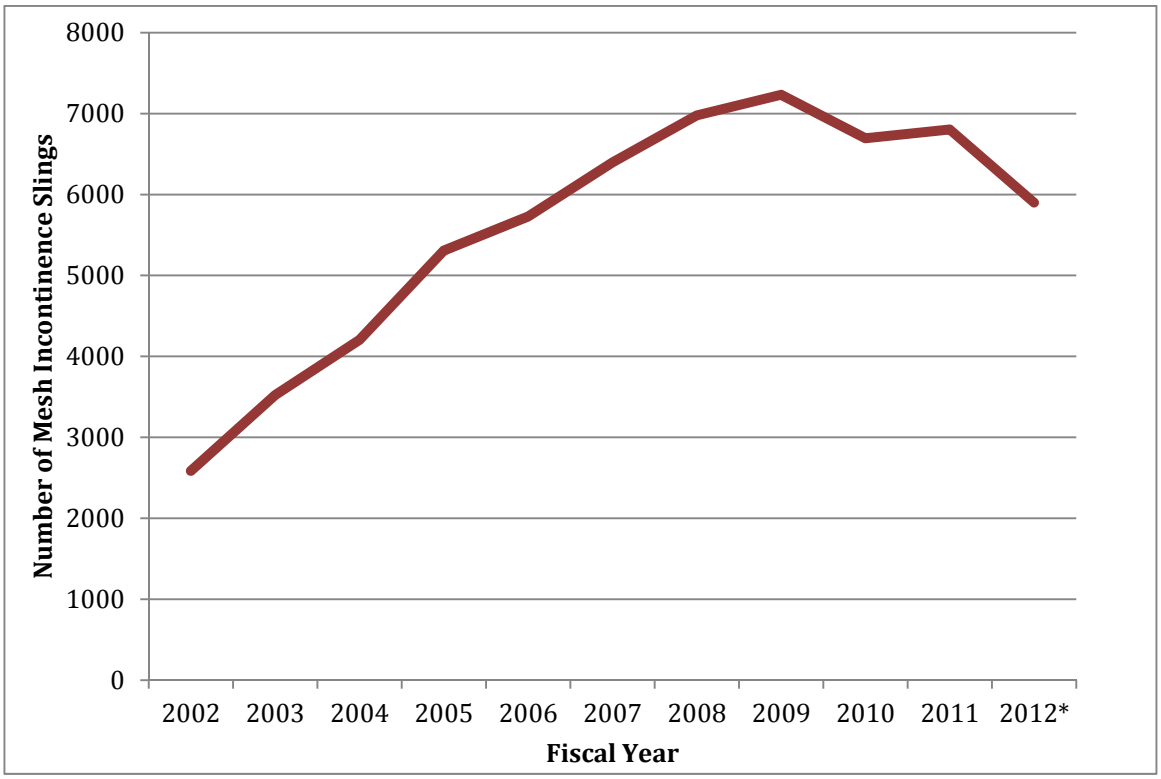
*****A multilevel model takes the hierarchical structure of the data into account. In this case patients were clustered within surgeons; a further level of clustering within hospitals was not added as these procedures are generally short stay cases, and the outcome is not likely to be influenced by routine short term hospital care.

eFigure 1. Flow Diagram of Cohort Selection



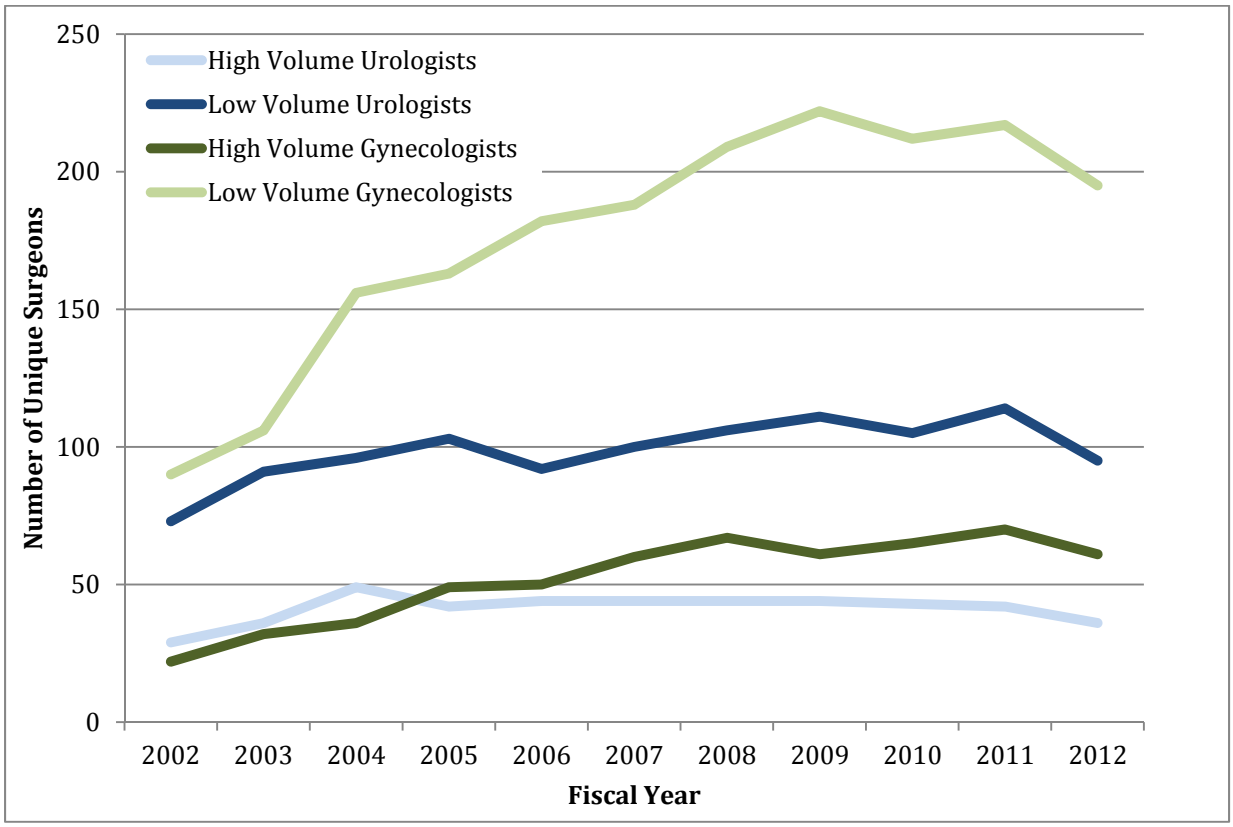
eFigure 2. Number of Mesh-Based Procedures for SUI Performed Yearly, 2002-2012

The declining number of overall synthetic incontinence slings (after 2009) follows the release of the FDA transvaginal mesh warning in October of 2008, and the Health Canada transvaginal mesh warning in February of 2010.



*As our study period ended Dec 31, 2012, the data for fiscal year 2012 (April 1 2012-March 30, 2013) was extrapolated for January 1 2013-March 30 2013 based on the prior 9 months of available data.

eFigure 3. Number of Surgeons Considered High Volume by Specialty, 2002-2012
High volume indicates ≥75th percentile for annual procedure volume. There were a total of 1068 surgeons during the study period, and within each year there were a median of 400 (IQR 364-446) surgeons performing these operations.



The increased number of "low volume" gynecologists is likely driven by a change in practice pattern as a result of increasing evidence suggesting that women should consider the prophylactic placement of a midurethral mesh sling at the time of prolapse repair (please see Wei JT, Nygaard I, Richter HE, et al. A midurethral sling to reduce incontinence after vaginal prolapse repair. *N Engl J Med*. 2012;366(25):2358–2367).

